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The illogic of *Kt/V*

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To the Editor: In reference to the recent articles regarding *Kt/V*,[1,2] a hemodialysis $Kt/V > 1.0$ implies there is complete removal of urea from a volume of body water which exceeds the total volume of water in the body, an impossibility, occurring because it measures dialyzer, not patient, clearance.

Kt/V for peritoneal dialysis is based on the actual amount of urea removed, explaining the discrepancy between the recommended weekly *Kt/V* in hemodialysis patients, 3.6 (3×1.2)–4.2 (3×1.4), compared to the weekly *Kt/V* in peritoneal dialysis patients, 1.7–2.0.[3] If the urea reduction ratio (URR) represents the actual amount of urea removed per hemodialysis treatment, with three sessions in a week, each with a urea reduction ratio of 0.65–0.70, would remove about 1.95–2.1 times the total body urea content, nearly identical to the recommended weekly *Kt/V* for peritoneal dialysis.

Kt/V is a flawed concept as used in hemodialysis and results in a fictitious and questionably meaningful number, but does have a useful role in peritoneal dialysis. URR more accurately reflects solute removal.

1. Spalding EM, Chandna SM, Davenport A *et al.* Kt/V underestimates the hemodialysis dose in women and small men. *Kidney Int* 2008; **74**: 348–355.
2. Lowrie EG. Prescribing and monitoring hemodialysis dose. *Kidney Int* 2008; **74**: 262–264.
3. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. *Am J Kidney Dis* 2006; **48**(Suppl 1): S2–S175.

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Response to 'The illogic of *Kt/V*'

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I agree completely with Dr Jenkins' impression that *Kt/V* is clinically illogical for reasons explained in the Commentary he cites.[1] In addition, Eloot *et al.* have recently found better urea removal when patients are treated for a longer time (*t*) despite comparable *Kt/V*.[2] Those data illustrate one more reason why *K*, *t*, and *V* should not be combined as a single ratio; we have one more fact indicating the clinical 'illogic of *Kt/V*'.

I respectfully disagree with his reason, however, because $Kt/V > 1.0$ does not indicate complete urea removal. The fact is revealed by his claim that urea reduction ratio (URR) reflects solute removal better than *Kt/V*. Urea kinetic equations prove that URR and *Kt/V* are tightly linked as the following illustrates:

(1) BUN at end of dialysis (C_t) = predialysis concentration (C_O) $\times e^{-Kt/V}$, so
(2) $C_t/C_O = e^{-Kt/V}$, and
(3) $URR = 100 \times (C_O - C_t)/C_O = 100 \times (1 - C_t/C_O)$, so
(4) $URR = 100 \times (1 - e^{-Kt/V})$.

Therefore, URR and *Kt/V* can be calculated from each other and one cannot reasonably argue in the same breath that URR is appropriate but *Kt/V* is not.

This example shows that $Kt/V = 0.5 \rightarrow URR = 39\%$, $Kt/V = 1.0 \rightarrow URR = 63\%$, and $Kt/V = 1.5 \rightarrow URR = 78\%$. Note also that $URR = 99\% \leftarrow Kt/V = 4.6$, $URR = 99.9\% \leftarrow Kt/V = 6.9$, and $URR = 99.99\% \leftarrow Kt/V = 9.2$. So, although *Kt/V* is not appropriate for evaluating clinical outcome,[1] it does reflect that URR and $Kt/V > 1.0$ is perfectly logical.

The confusion probably evolved from misleading statements suggesting *Kt/V* reflects a 'fractional clearance' of urea. For example, we find,

"To normalize for differences in the size and habitus of patients, a dose of hemodialysis (prescribed or delivered) is best described as the *fractional clearance* of urea as a function of its distribution volume (*Kt/V*)".[3] (Emphasis added)

Such unclear statements likely suggested to many that when, for example, $Kt/V = 48\,l/40\,l = 1.2$ the 'fractional clearance' would be 120%, so those 40 l should be completely 'cleared'. Unfortunately, the concept is incorrect as I hope I have shown.

1. Lowrie EG. Prescribing and monitoring hemodialysis dose. *Kidney Int* 2008; **74**: 262–264.
2. Eloot S, Van Biesen W, Dhondt A *et al.* Impact of hemodialysis duration on the removal of uremic retention solutes. *Kidney Int* 2008; **73**: 765–770.
3. NKF K/DOQI Guidelines 2000, Guideline #2: Method of Measurement of Delivered Dose of Hemodialysis (Evidence) http://www.kidney.org/PROFESSIONALS/kdoqi/guidelines_updates/doqi_uptoc.html.

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Response to 'The illogic of *Kt/V*'

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Our paper[1] was not intended to praise the *Kt/V* concept of dialysis adequacy but to provide some constructive criticism. Jenkins raises some theoretical issues that relate to the validity of the whole *Kt/V* concept in the hemodialysis setting, whereas our paper drew attention to potential problems with the concept of using *V*, an estimate of total body water, to normalize estimated urea clearance. We provided some support for the use of a normalizing factor, which better reflects metabolic activity.

There are a number of issues. First, whether any measure of urea removal is sufficient to judge dialysis

adequacy; second, if a measure of urea removal were to be used, whether a simple urea reduction ratio is acceptable or whether a measure that incorporates a normalizing factor is necessary; and finally – whether the widespread use of *V* as this normalizing factor is valid. Jenkins' criticisms relate to the second point whereas our paper addressed the third.

Focusing solely on normalized urea clearance presents a flawed view of dialysis adequacy. There are many other facets. Middle molecule removal is important. Reanalysis of data from the HEMO study has demonstrated that retention of β_2 microglobulin was associated with increased mortality.[2] In addition to solute clearances, dialysis prescription encompasses other goals, including sodium and water, divalent ion and acid-base homeostasis. Dialysis hypotension is more likely to occur when dialysis session time is shortened, because of increased ultrafiltration rates, and failure to achieve adequate sodium removal with increased interdialytic weight gains.

Although we have criticized the appropriateness of the use of *Kt/V* in prescribing hemodialysis, we do believe that an assessment of the amount of dialysis delivered is vital, unless very long and/or very frequent dialysis sessions are employed. Normalized urea clearance, although not perfect, is a useful marker of adequacy, though we believe it could be used more astutely. Our paper proposes that the normalizing factor should reflect metabolic activity, as use of *V* may risk under-dialysis in women and small men. We suggest that this should be borne in mind while we continue to use *Kt/V*, and that the adequacy targets should be adjusted in these two groups.

1. Spalding EM, Chandna SM, Davenport A *et al.* Kt/V underestimates the hemodialysis dose in women and small men. *Kidney Int* 2008; **74**: 348–355.
2. Cheung AK, Rocco MV, Yan G *et al.* Serum beta-2 microglobulin levels predict mortality in dialysis patients: results of the HEMO study. *J Am Soc Nephrol* 2006; **17**: 546–555.

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Lipid disorders in experimental chronic kidney disease: a role for SREBPs

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To the Editor: We have read with interest the article by Hai-Lu Zhao *et al.*[1] on fat redistribution and adipocyte transformation in uninephrectomized rats. Among numerous interesting findings, the authors demonstrate increased ectopic fat deposits in remnant kidneys and other solid organs of chronic kidney disease animals. The authors speculate on the possible mechanisms, taking into account increased lipid production. This hypothesis is strengthened by demonstrating that expression of HMG-CoA reductase, the rate-limiting enzyme in cholesterologenesis pathway, is increased in remnant kidneys.

We would like to confirm these results and highlight the potential role of sterol regulatory element-binding proteins (SREBPs) in the above-mentioned disturbances. SREBPs are nuclear transcription factors that are currently regarded as the major regulators of both cholesterologenesis and lipogenesis.

We have shown that both gene expression and protein abundance of SREBPs are increased in white adipose tissue[2] and livers[3] of chronic kidney disease rats. Moreover, increase in SREBP expression has been demonstrated in kidneys of diabetic mice[4] and in experimental age-related nephropathy,[5] where it has been clearly linked to lipid deposition in glomeruli, and consequently to mesangial expansion, glomerulosclerosis, and proteinuria.

These results complement the findings demonstrated by Zhao *et al*. as they bring us closer to elucidating the issue of altered lipid metabolism in the course of chronic kidney disease.[3]

1. Zhao HL, Sui Y, Guan J *et al.* Fat redistribution and adipocyte transformation in uninephrectomized rats. *Kidney Int* 2008; **74**: 467–477.
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3. Szolkiewicz M, Chmielewski M, Nogalska A *et al.* The potential role of sterol regulatory element binding protein transcription factors in renal injury. *J Ren Nutr* 2007; **17**: 62–65.
4. Sun L, Halaihel N, Zhang W *et al.* Role of sterol regulatory element-binding protein 1 in regulation of renal lipid metabolism and glomerulosclerosis in diabetes mellitus. *J Biol Chem* 2002; **277**: 18919–18927.
5. Jiang T, Liebman SE, Lucia MS *et al.* Role of altered renal lipid metabolism and the sterol regulatory element binding proteins in the pathogenesis of age-related renal disease. *Kidney Int* 2005; **68**: 2608–2620.

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Response to 'Lipid disorders in experimental chronic kidney disease: a role for SREBPs'

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We thank Chmielewski *et al.* for drawing attention to the potential role of sterol regulatory element-binding